

REMARKS

In the Office Action mailed August 31, 2005, restriction was required as between:

Group I (Claims 1-7 and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is selected from the group consisting of ATCC 39961 and ATCC 39962;

Group II (Claims 1-6, 13-14 and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is ATCC 67923;

Group III (Claims 1-6, 13, 15-16 and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is selected from the group consisting of ATCC 55117 and ATCC 55115;

Group IV (Claims 1-5, 8 and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is selected from the group consisting of ATCC 53865 and ATCC 53866;

Group V (Claims 1-5, 11-12, and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is selected from the group consisting of ATCC 55110, and ATCC 55115, ATCC 55113, ATCC 55119, and ATCC 55118; and

Group VI (Claims 1-5, 9-10 and 22-34) drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is selected from the group consisting of ATCC 67537, ATCC 53681, ATCC 67538, ATCC 53680, ATCC 53678 and ATCC 67813.

The Examiner reasoned as follows:

"Inventions I and any of II-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP §808.01). The instant specification does not disclose that these methods would be used together. The method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is *Salmonella typhimurium* selected from the group consisting of ATCC 39961 and ATCC 39962 and any other method, such as the method of group II, is unrelated as they utilize different function and mode of operation. Each invention performs this function using a structurally and functionally divergent material. Moreover, the different enteropathogenic bacteria differ significantly within each of the methods. These bacterial strains within the methods constitute patentably distinct inventions. For instance, the groups are directed to different enteropathogenic bacterium which are distinct physically, structurally, and functionally and are therefore patentably distinct, each

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group from the other, and one bacterium is not required to practice the other. Each group comprises separate and distinct strains that do not share a substantial structural feature disclosed as being essential to the utility of the invention. For instance only group III comprises strains of *Salmonella typhi* which have been made avirulent by an inactivating mutation in the structural *crp* gene. Therefore, each method is unrelated. For these reasons the Inventions I and any of II-VI are patentably distinct. (Office Action dated August 31, 2005, pages 3-4.)

Applicant disagrees. The present invention relates to novel methods of delivering a protein of interest to poultry and other domesticated birds (hereinafter "poultry"). The protein, *e.g.* a growth factor or heterologous gene product, is administered by *whole-body spraying of the poultry* with an effective amount of a live avirulent derivative of an enteropathogenic bacterium that contains/encodes a recombinant gene that encodes for the expression of the protein of interest. That is, the avirulent derivative of the enteropathogenic bacterium serves as a vector to deliver the protein of interest to the gut of a domestic bird.

Preferred enteropathogenic bacteria to be used as avirulent derivative carrier organisms (or vectors) of the present invention are *Salmonella* species, and due to the nature of the spray application, it is preferred that the enteropathogenic bacterium is other than one that causes respiratory disease in birds.

The present invention offers numerous advantages over the prior art, most notably, the present invention can be used to effectively deliver a protein in a large scale to *newly hatched* chicks. It is known that newly hatched chicks often do not eat or drink for up to several days after hatching; therefore, protein delivery methods involving the feed medium or drinking water are ineffective. The present invention, on the other hand, may be used to deliver selected proteins to domestic poultry in a manner that is easy and inexpensive to administer under normal commercial poultry conditions, and is effective for delivering the proteins to newly hatched chicks in an efficient manner and without individual handling.

In restricting the present claims, the Examiner directs Applicant's attention to MPEP §806.04 and states:

The instant specification does not disclose that these methods would be used together. The method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is *Salmonella typhimurium* selected from the group consisting of ATCC 39961 and ATCC 39962 and any other method, such as the method of group II, is **unrelated as they utilize different function and mode of operation.**

There are no differences in function or mode of operation. In the claimed method, the enteropathogenic bacterium **always** functions as the **vector** for the protein or antigen, *i.e.*, the particular bacterium merely

vectors the desired protein to the gut of the domestic bird, more preferably, to the gut associated lymphoid tissue (GALT). No matter which avirulent derivative of an enteropathogenic bacterium is chosen to vector the desired protein, it functions in the same way through the same mode of operation: that is, the microorganism vectors the protein to the gut of the domestic bird.

Applicant points out that all the cited strains are known in the art. As is evident from the specification, the deposited strains recited in the claims (*i.e.*, ATCC 39961, ATCC 39962, ATCC 67923, ATCC 55117, ATCC 55115, ATCC 53865, ATCC 53866, ATCC 55110, ATCC 55113, ATCC 55119, ATCC 55118, ATCC 67537, ATCC 53681, ATCC 67538, ATCC 53680, ATCC 53678, and ATCC 67813), which are deemed a basis for separation into different restriction groups, ALL belong to the following category: “an avirulent derivative of an enteropathogenic bacterium...other than one that causes respiratory disease in birds.” The differences in the particular bacterium relate to the particular mutations to make the bacterium *avirulent*. The mutations are neither related to nor essential to the role of the bacterium **as a vector** in the claimed method of delivering a protein to a domestic bird comprising:

administering to the bird in a whole-body spray an effective amount of a live avirulent derivative of an enteropathogenic bacterium comprising a recombinant gene that codes for the expression of the protein, wherein  
(a) the enteropathogenic bacterium is other than one that causes respiratory disease in birds, (b) the protein is delivered to the bird, and  
(c) the spray is composed of droplets having a mean diameter of 40-200 microns.

That is to say, the differences between the strains of the different groups have nothing to do with the invention; they only recite particular embodiments encompassed by the same invention.

Moreover, contrary to the Examiner's assertions, MPEP §806.04 actually states:

"If it can be shown that the two or more inventions are in fact independent, applicant should be required to restrict the claims presented to but one of such independent inventions. For example:

(A) Two different combinations, not disclosed as capable of use together, having different modes of operation, different functions or different effects are independent. An article of apparel such as a shoe, and a locomotive bearing would be an example. A process of painting a house and a process of boring a well would be a second example.

In stark contrast to the example of a proper restriction between claims to methods of painting a house and boring a well, Applicants' claims **all relate to a method of administering a protein to**

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**poultry via the same step of whole-body spray application of a solution containing an enteropathogenic bacterium expressing the protein.** Applicant notes that Claim 1 is clearly a linking claim as it is the main claim of each of the Examiner's six invention groups: It is clear that Claim 1 is independent of the bacterium chosen. Moreover, Applicant notes that Claim 1 has already been patented in the parent case. *See, e.g.*, US Patent No. 6,866,847:

1. A method of delivering a protein to a domestic bird comprising administering to the bird in a whole body spray an effective amount of a live avirulent derivative of an enteropathogenic bacterium comprising a recombinant gene that codes for the expression of the protein, wherein
  - (a) the enteropathogenic bacterium is other than one that causes respiratory disease in birds, (b) the protein is delivered to the bird, and (c) the spray is composed of droplets having a mean droplet size of 40 to 200 microns.

At the end of prosecution of the parent case, Applicant requested the rejoinder of the remaining dependent claims (which merely specified the particular strains of avirulent enteropathogens encompassed by the allowed main claim) by way of a Rule 312 amendment; however, the Examiner refused to consider the amendment, making the filing of the present divisional necessary. The failure of the Examiner to acknowledge that the particular deposited strains are species of the genus "avirulent derivative of an enteropathogenic bacterium" has caused a double patenting paradox, in that Claim 1 of US Pat. No. 6,866,847 and Claim 1 of the present application have been determined to be directed to separate invention even though they are identically worded. To persist in the present restriction requirement will only compound the situation: Applicant will ultimately obtain several patents, all having an identical Claim 1. The Examiner may only resolve this paradox by removing the restriction requirement and requiring linkage to these claims of the parent case (which Applicant tried to establish via the Rule 312 amendment that was refused entry).

#### Conclusion and Provisional Election

Applicant submits that in view of the foregoing remarks all the claims herein are seen to relate to a single inventive concept, and the claims are in a form and are of the sort that is properly viewed as relating to a single invention that should not be restricted. Applicants request that the restriction requirement of the Office Action of August 31, 2005 be reconsidered and withdrawn.

Although, for reasons set forth above, Applicants believe that the restriction is improper and uncalled for, and without in any way acquiescing in the reasons for the requirements set forth in the

Office Action, but in order to be fully responsive to the Office Action, Applicants provisionally elect for examination the claims of Group II, i.e., Claims 1-6, 13-14 and 22-34.

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date

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